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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,984	03/19/1999	ARMIN PETER CZERNILOFSKY	0652.1830000	3631

7590 12/21/2006
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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/202,984

Applicant(s)

CZERNILOFSKY ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61,63-90 and 92-126 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 61,63-90 and 92-126 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 November 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 17, 2006 has been entered.

Status of the Application

2. The action is in response to the RCE filed on October 17, 2006. Currently claims 61, 63-90 and 92-126 are pending. Claims 1-60, 62, 91 are cancelled. Claims 61 and 90 are amended. All arguments and amendment have been fully considered and thoroughly reviewed and deemed unpersuasive for the reasons that follow. The newly amended claims recite new limitations that did not change the scope of the claims. To address the new limitations the rejections made in the previous office action are re-written herein to include new claim limitations.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 61, 67-69, 74-76, 81-85, 87-89, 121, 123-124 are rejected under 35 U.S.C. 102(b) as being anticipated by Weyer et al. (Receptors and Channels Vol. 1, pp. 193-200, 1993).

Weyer et al. teach high throughput parallel screening method (multiple well -format) of claims 61, of determining the pharmacological effect of a substance (test substance) on the activity of different biological target molecules (Nk2 receptor, 5-HT2 receptor) contained in test cells of same type (transformed human adenocarcinoma cell line clones) (see page 199, col. 2, paragraph 1-2), comprising

(a) selecting from a cell population test cells of the same type which contain different molecules (selecting clones of transformed human adeno carcinoma cell line having different gene targets (Nk2, 5-HT2 receptors, see page 199, col. 2, paragraph 1-2, page 194, col. 2, paragraph 2, page 196, col. 1, paragraph 1-2)

(b) applying from the same supply (from the same supply solution of phorbol ester PMA) a defined amount (10ng/ml) of a test substance (phorbol ester PMA) in one operation (simultaneously) to more than one test cells of the same type comprising more than one cellular substrates (receptors), which differ in that they contain different target molecules (different receptors) (see page 199, col. 2, paragraph 1 under Luciferase assays, indicating treating isolated clones seeded in a 96 well format with a test compound);

(b) measuring the effect of the substance on the biological activities of said different target molecules using a detection system using different assays or assay format for each cellular substrate (measuring the expression of luciferase gene, Nk2 receptor and 5-HT2 receptor) (see page 199, col. 2, paragraph 1 under luciferase assays, see page 200, col. 1, paragraph 1, indicating measuring the activities using luminometer, and ion exchange chromatography);

(c) directly or indirectly comparing the effect of said test substance on the biological activities of said different target molecules, wherein target molecules comprise receptor-coupled

signal transduction pathway (see page 195, col. 2, paragraph 1, page 196, col. 1, paragraphs 1-2, col. 2, paragraphs 1-3, page 197, col. 1, line 1-10, paragraph 1, col. 2, paragraph 1).

With regard to claims 67-69, 74-76, Weyer et al. teach that said different target molecules include Nk1, Nk-2, Nk3, serotonin receptors, etc. (see page 196, col. 1, paragraphs 1-2, col. 2, paragraph 1, page 199, col. 2, paragraph 1 under luciferase assays);

With regard to claim 81-82, Weyer et al. et al. teach that said test cells are transformed with DNA operably encoding with different receptor molecules (see page 199, paragraph 1 and cell culture and transfections section, page 194, col. 1, paragraph 2).

With regard to claim 83-85, Weyer et al. teach that the detection system comprises luciferase reporter system (see page 199, col. 2, paragraph 1 under luciferase assays).

With regard to claims 87-89, Weyer et al. teach that said test cells comprise human cells having same genotype (human adenocarcinoma cell line) (see page 199, col. 2, paragraph 1 under cell culture and transfections section).

With regard to claims 121, 123-124, Weyer et al. teach that said test cells are clonally selected from a single cell, using G-418 antibiotic resistance marker (see page 199, col. 2, paragraph 1 under cell culture and transfections). Accordingly Weyer et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 63-64, 66, 70, 77-80, 90, 92-93, 95-99, 103-114, 116-120, 122, 125-126 rejected under 35 U.S.C. 103(a) as being unpatentable over Weyer et al. (Receptors and Channels Vol. 1, pp. 193-200, 1993) in view of Johnson (WO95/28421).

Weyer et al. teach high throughput parallel screening method (multiple well -format) of claims 61, of determining the pharmacological effect of a substance (test substance) on the activity of different biological target molecules (Nk2 receptor, 5-HT2 receptor) contained in test cells of same type (transformed human adenocarcinoma cell line clones) (see page 199, col. 2, paragraph 1-2), comprising

(a) selecting from a cell population test cells of the same type which contain different molecules (selecting clones of transformed human adenocarcinoma cell line having different gene targets (Nk2, 5-HT2 receptors, see page 199, col. 2, paragraph 1-2, page 194, col. 2, paragraph 2, page 196, col. 1, paragraph 1-2)

(b) applying from the same supply (from the same supply solution of phorbol ester PMA) a defined amount (10ng/ml) of a test substance (phorbol ester PMA) one operation

(simultaneously) to more than one test cells of the same type comprising more than one cellular substrates (receptors), which differ in that they contain different target molecules (different receptors) (see page 199, col. 2, paragraph 1 under Luciferase assays, indicating treating isolated clones in a 96 well format with a test compound)

(b) measuring the effect of the substance on the biological activities of said different target molecules using a detection system using different assays or assay format for each cellular substrate (measuring the expression of luciferase gene, Nk2 receptor and 5-HT2 receptor) (see page 199, col. 2, paragraph 1 under luciferase assays, see page 200, col. 1, paragraph 1, indicating measuring the activities using luminometer, and ion exchange chromatography);

(c) directly or indirectly comparing the effect of said test substance on the biological activities of said different target molecules, wherein target molecules comprise receptor-coupled signal transduction pathway (see page 195, col. 2, paragraph 1, page 196, col. 1, paragraphs 1-2, col. 2, paragraphs 1-3, page 197, col. 1, line 1-10, paragraph 1, col. 2, paragraph 1).

With regard to claims 96-98, 103-105, Weyer et al. teach that said target molecule includes receptor-coupled signal transduction pathway comprising different target molecules include Nk1, Nk-2, Nk3, serotonin receptors, etc. (see page 196, col. 1, paragraphs 1-2, col. 2, paragraph 1, page 199, col. 2, paragraph 1 under luciferase assays);

With regard to claim 110-111, Weyer et al. et al. teach that said test cells are transformed with DNA operably encoding with different receptor molecules (see page 199, paragraph 1 and cell culture and transfections section, page 194, col. 1, paragraph 2).

With regard to claim 112-114, Weyer et al. teach that the detection system comprises luciferase reporter system (see page 199, col. 2, paragraph 1 under luciferase assays).

With regard to claims 116-117, 120, Weyer et al. teach that said test cells comprise human cells having same genotype (human adenocarcinoma cell line) (see page 199, col. 2, paragraph 1 under cell culture and transfections section) and normal cells (see page 194, col. 2, paragraph 2).

With regard to claims 122, 125-126, Weyer et al. teach that said test cells are clonally selected from a single cell, using G-418 antibiotic resistance marker (see page 199, col. 2, paragraph 1 under cell culture and transfections).

However, Weyer et al. did not teach target molecules comprising Ras, Raf, receptors as EGF, biological activity comprising proliferation, apoptosis, same cell types with a different states of differentiation or activation.

Johnson teaches a method of claims 63-64, 66, 69-70, 77-80, 90, 92-93, 95, 98-99, 106-109, of determining the pharmacological effect of a substance (test substance) on the activity of different biological target molecules in the signal transduction pathway wherein said different target molecules, wherein target molecules comprise receptor-coupled signal transduction pathway (see page 61, line 16-28, page 62, line 1-22).

With regard to claims 63-64, 67-71, 74-76, 92-93, 96-100, 103-105, Johnson teaches that said different target molecules include Ras, Raf, tyrosine kinase receptors serotonin receptors, human growth hormone receptors, neurokinin receptors 1,2 (tachykinin receptors) EGF etc. (see page 5, line 1-9, page 17, line 1-16);

With regard to claims 77-80, 106-109, Johnson teaches that the biological activity is a pathological effect including proliferation, or apoptosis (see page 6, line 9-24, page 18, line 21-28, page 19, line 1-28, page 20, line 1-28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Weyer et al. with a step of including cells comprising various signaling molecules that control cell differentiation/ growth/ apoptosis as taught by Johnson to achieve an enhanced sensitivity in evaluating the effect of a substance on the regulation of signal transduction pathway dependent cell differentiation / cell death or apoptosis because Johnson explicitly taught that the growth and differentiation are tightly regulated by signal transduction pathways within cells, which maintain the balanced steady state functioning of a cell and any break down in the signal transduction in a cell would lead to disease states that disturb the cellular functions (see page 6, line 9-24). An ordinary practitioner would have a reasonable expectation of success that the combination of method of Weyer et al. with cells comprising target molecules of signal transduction pathway as taught by Johnson would result in evaluating the effect of a substance on the signal transduction pathway that directs the growth and differentiation within a cell and such a modification of the method is considered as obvious over the cited prior art.

B. Claims 65, 71-73, 94, 100-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weyer et al. (Receptors and Channels Vol. 1, pp. 193-200, 1993) in view of Johnson (WO95/28421) as applied to claims 63-64, 66, 70, 77-80, 90, 92-93, 95-99, 103-114, 116-120, 122, 125-126 above, and further in view of Bischoff et al. (USPN. 5,705,342) and Brown et al. (USPN. 5,929,081).

Weyer et al. in view of Johnson teach a high throughput parallel screening method as discussed in section 4A above.

However neither Weyer et al. nor Johnson teach the target molecules as Bcl-2, receptors as HGF, HER2, and KDR.

Bischoff et al. et al. teach regulation of cell proliferation control and neoplasia by Bcl-2 expression (see col. 3, line 2-48) and the signal transduction mediated by the association between Ras and bcl-2 (see col. 8, line 49-67).

Brown et al. teach method for treating diseases mediated by cellular proliferation signal transduction pathway effector molecules, wherein Brown et al. disclose that the method comprises treating the diseases associated with cellular target receptor molecules such as VEGF (kinin domain receptors (KDR)), HER2, 3, ras/Raf pathway signaling molecules (see col. 10, line 13-58).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Weyer et al. in view of Johnson with a step of including Bcl-2 as taught by Bischoff et al. and receptors as HGF, HER2 and KDR as taught by Brown et al. to enhance the sensitivity of the method to detect the signaling pathway as a whole because Bischoff et al explicitly taught the mediation of Ras in controlling bcl-2 function that regulates cell proliferation and neoplasia (see col. 3, line 2-48, col. 8, line 49-67). Further Brown et al. explicitly taught treating diseases mediated by cellular proliferation signal transduction pathway effector molecules, wherein Brown et al. disclose that the method comprises treating the diseases associated with cellular target receptor molecules such as VEGF (kinin domain receptors (KDR)), HER2, 3, ras/Raf pathway signaling molecules (see col. 10, line 13-58). An ordinary practitioner would have been motivated to combine the method of Weyer et al. in view of Johnson with Bcl-2 target molecule and receptors as HGF, HER2 and KDR as taught by Brown

et because an ordinary practitioner would have a reasonable expectation of success that the inclusion of various signal transduction pathway mediators would result in an enhanced method for determining the effect of a substance on the regulation of signal transduction that controls the cell differentiation and apoptosis and such a modification of the method is considered obvious over the cited prior art.

C. Claims 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weyer et al. (Receptors and Channels Vol. 1, pp. 193-200, 1993) in view of Chalfie et al. (USPN.5,491,084).

Weyer et al a high throughput parallel screening method as discussed in the section 4A above.

Weyer et al. did not teach green fluorescent protein as a reporter gene.

Chalfie et al. teach a method for cells expressing a biological activity (gene expression) of a particular target molecule, wherein the regulatory sequences of a target molecule are linked to a reporter fluorescent protein which fluoresces when said target is expressed within the cells (see column 1, lines 38-52). Chalfie et al. also teach that said reporter fluorescent protein is a gene encoding a green fluorescent protein (column 1, lines 38-41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of determining the effect of a substance on the biological activities on target molecules as taught by Weyer et al. with the method of detecting effect of a substance on different target molecules linked to a GFP reporter gene system as taught by Chalfie et al. to achieve an enhanced sensitivity in determining the effect of a substance on the biological activity or activities because Chalfie et al. taught that the biological activity of a particular target molecule in response to an external stimulus can be monitored within the cells

containing the target by the expression of green fluorescence protein linked to said target and the cells expressing the GFP can be easily selected and sorted by a fluorescent-activated sorter (see column 4, lines 3-12). Therefore an ordinary practitioner would have a reasonable expectation of success that the combination of the reporter gene mediated detection method of determining the effect of a substance on the biological activity as taught by Weyer et al. with the method of selecting or localizing a biological activity within the cells using the reporter gene encoding a green fluorescent protein as taught by Chalfie et al. would result in enhance the detection of the biological activity of a target molecule within the cells, so as to detect and sort the cells expressing the target molecules without lysing the cells and such modification of the method is obvious over the cited prior art.

D. Claim 115 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weyer et al. (Receptors and Channels Vol. 1, pp. 193-200, 1993) in view of Johnson (WO95/28421) as applied to claims 63-64, 66, 70, 77-80, 90, 92-93, 95-99, 103-114, 116-120, 122, 125-126 above, and further in view of Chalfie et al. (USPN.5,491,084).

Weyer et al in view of Johnson teach a high throughput parallel screening method as discussed in the section 4A above.

Neither Weyer et al. nor Johnson teach green fluorescent protein as a reporter gene.

Chalfie et al. teach a method for cells expressing a biological activity (gene expression) of a particular target molecule, wherein the regulatory sequences of a target molecule are linked to a reporter fluorescent protein which fluoresces when said target is expressed within the cells (see column 1, lines 38-52). Chalfie et al. also teach that said reporter fluorescent protein is a gene encoding a green fluorescent protein (column 1, lines 38-41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of determining the effect of a substance on the biological activities on target molecules as taught by Weyer et al. in view of Johnson with the method of detecting effect of a substance on different target molecules linked to a GFP reporter gene system as taught by Chalfie et al. to achieve an enhanced sensitivity in determining the effect of a substance on the biological activity or activities because Chalfie et al. taught that the biological activity of a particular target molecule in response to an external stimulus can be monitored within the cells containing the target by the expression of green fluorescence protein linked to said target and the cells expressing the GFP can be easily selected and sorted by a fluorescent-activated sorter (see column 4, lines 3-12). Therefore an ordinary practitioner would have a reasonable expectation of success that the combination of the reporter gene mediated detection method of determining the effect of a substance on the biological activity as taught by Weyer et al. in view of Johnson with the method of selecting or localizing a biological activity within the cells using the reporter gene encoding a green fluorescent protein as taught by Chalfie et al. would result in enhance the detection of the biological activity of a target molecule within the cells, so as to detect and sort the cells expressing the target molecules without lysing the cells and such modification of the method is obvious over the cited prior art.

Response to arguments:

5. With regard to the objection to the claims, Applicants' amendment and arguments are fully considered and found persuasive. The objection is withdrawn herein in view of the amendment.
6. With regard to the rejection of claims 61, 67-69, 74-76, 81-85, 87-89, 121, and 123-124, under 35 USC 102(b) as being anticipated by Weyer et al., Applicants' arguments and amendment are

fully considered and found unpersuasive. Applicants' argue that Weyer et al. does not teach applying a test substance in one operation and argue that Weyer et al. teaches a comparative screen in which the same cells with the same receptors underwent different tests. Applicants' arguments are fully considered and found unpersuasive because the instant specification does not define one operation, further given the broadest reasonable interpretation, applying a test substance simultaneously to test cells in a 96 well format does not exclude the scope of the limitation 'applying a test substance in one operation'. Further the same cells (adenocarcinoma cells) comprise different biological target molecules, that is, the same cell line is transfected with different receptor containing plasmids and the clones containing said different target molecules are isolated, thus the assertion that the same cells having same receptors is not persuasive. Applicants' further argue that Weyer et al. teach various comparisons made from tests comprising more than one operation or multiple tests. The arguments are found unpersuasive because the Materials and methods section on page 199 clearly teach application of a test substance in one operation and assaying for the expression of different receptors in the cells treated with the test substance. The Applicants cited page 196 of Weyer et al., which discusses the results of the experiment according to the protocol on page 199. Thus the results show comparisons of results from said method on page 199. In addition the claim 61 requires different assay formats which is supported by the disclosure of Weyer et al. performing different receptor assays. Further Applicants' point out the paragraphs of the instant specification for defining the concept of 'parallel screening' and argue that Weyer et al. does not teach the limitation 'one operation' that is required by the instant claims and assert that at least for that crucial aspect Weyer et al. does not anticipate the instant claims. Applicants' arguments are fully considered

and found unpersuasive. As discussed above simultaneous application of the same test substance to different cellular substrates in a 96-well format does encompass the limitation 'one operation' and the cited paragraphs of the specification describes the concept of parallel screening which is equivalent to the 96-well format taught by Weyer et al. but does not define 'one operation' and since there exists no definition for 'one operation', the instant claims do not exclude the teachings of Weyer et al. applying a test substance simultaneously to more than one test cells. Therefore the rejection is maintained herein.

7. With regard to the rejection of claims 61, 63, 64, 66, 70, 77-80, 92, 93, 95-99, 103-114, 116-120, 122, 125, as being obvious over Weyer et al. in view of Johnson, Applicants' arguments and amendment are fully considered and found unpersuasive. Applicants argue that Weyer et al. does not teach the limitations in the independent claims as discussed above and the teaching of Johnson et al. does not remedy the deficiencies of Weyer et al. and does not render the instant invention obvious. Applicants' arguments are fully considered and found unpersuasive. As discussed above Weyer et al. does teach the limitations in the instant claims and as discussed in the rejection above it is obvious to combine the teachings of Weyer et al. with the teachings of Johnson et al. to render that the instant claims are obvious. Therefore the rejection is maintained.

8. With regard to the rejection of claims 65, 71-73, 94, and 100-102 as being obvious over Weyer et al. in view of Johnson and further in view of Bischoff and Brown, Applicants' arguments and amendment are fully considered and found unpersuasive. Applicants argue that Weyer et al. in view of does not teach the limitations in the independent claims as discussed above and the teaching of Bischoff and Brown does not remedy the deficiencies of Weyer et al. in view of Johnson et al. and does not render the instant invention obvious. Applicants'

arguments are fully considered and found unpersuasive. As discussed above Weyer et al. in view of Johnson et al. does teach the limitations in the instant claims and as discussed in the rejection above it is obvious to combine the teachings of Weyer et al. in view of Johnson et al. with the teachings of Bischiff and Brown to render that the instant claims are obvious. Therefore the rejection is maintained.

9. With regard to the rejection of claim 86, as being obvious over Weyer et al. in view of Chalfe et al., Applicants' arguments and amendment are fully considered and found unpersuasive. Applicants argue that Weyer et al. does not teach the limitations in the independent claims as discussed above and the teaching of Chalfe does not remedy the deficiencies of Weyer et al. and does not render the instant invention obvious since Chalfe merely teaches the use of GFP as a reporter gene. Applicants' arguments are fully considered and found unpersuasive. As discussed above Weyer et al. does teach the limitations in the instant claims and as discussed in the rejection above it is obvious to combine the teachings of Weyer et al. with the teachings of Chalfe directed to the explicit use of GFP as a reporter gene to render the instant claims are obvious. Therefore the rejection is maintained.

10. With regard to the rejection of claim 115, as being obvious over Weyer et al. in view of Johnson and further in view of Chalfe et al., Applicants' arguments and amendment are fully considered and found unpersuasive. Applicants argue that Weyer et al. in view of Johnson et al. does not teach the limitations in the independent claims as discussed above and the teaching of Chalfe does not remedy the deficiencies of Weyer et al. in view of Johnson et al. and does not render the instant invention obvious. Applicants' arguments are fully considered and found unpersuasive. As discussed above Weyer et al. in view of Johnson et al. does teach the

limitations in the instant claims and as discussed in the rejection above it is obvious to combine the teachings of Weyer et al. in view of Johnson et al. with the teachings of Chalfe directed to the explicit use of GFP as a reporter gene to render the instant claims are obvious. Therefore the rejection is maintained.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru
SURYAPRABHA CHUNDURU
PRIMARY EXAMINER
12/19/06